中文題目：半乳醣凝集素-1 在壓力超負荷引起之心臟衰竭中扮演保護角色

英文題目：Galectin-1 plays essential protective role in pressure overload-induced heart failure

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Background*:* Heart failure (HF) is a leading cause of mortality and mobility worldwide. However, the precise mechanism of the transition from compensatory remodeling to decompensation in HF progression remains largely unknown. Recent study indicated the protective role of Galectin-1 (gal-1), a member of an evolutionary conserved family of β-galactosides-binding lectins, in adverse cardiac remodeling in acute myocardial infarction. Here, we examine the role of gal-1 in maladaptive remodeling and HF in pressure-overload animal model.

Method*:* Murine pressure-overload model with transverse aortic constriction (TAC), Echocardiography, immunohistochemical analysis of autophagic flux, ER (endoplasmic reticulum) stress and apoptosis, cyclic mechanical stretch on cultured cardiac myocytes and Western blot assay.

Result*:* We firstly demonstrated that gal-1 knock-out (KO) mice significantly increased diffuse myocardial fibrosis (with both picrosirius red and masson stains) and chamber dilation, compared to wild-type (WT) mice subjected to TAC for 1 week.

All gal-1 KO mice in response to TAC died of HF within 1 week. In contrast, WT mice were still alive until 3 weeks after TAC. Echocardiography showed significantly impaired LV systolic function in gal-1 KO mice in contrast to preserved systolic function in WT mice 1 week after TAC.

Both immunohistochemistry and western blot revealed gal-1 ablation markedly suppressed autophagic flux (with accumulation of LC3 and p62) and concomitantly aggravated ER stress (with increased GRP78 and p-eIF2α protein expression) and apoptosis (by TUNAL assay and increased cytochrome c, caspase 9 & 3 and cleaved PARP protein expression) in myocardial muscle cells, compared to WT animals 1 week after TAC.

In in-vitro study, using fluorescence microscopy following cells transfected with tandem fluorescent GFP-RFP-LC3 construct, we further showed that the number of autophagolysosomes significantly decreased in cultured gal-1-deficient cardiomyocytes derived from HL-1 cell line under cyclic mechanical stretch, suggesting that gal-1 is involved in the fusion process between autophagosomes and lysosomes.

Conclusion*:* Our study implicates that Galectin-1 plays pivotal role in protecting against pressure overload-induced heart failure via promotion of myocardial autophagic flux, and subsequent suppression of ER stress and apoptosis. These findings may provide novel therapeutic strategy for heart failure.